(FILE 'HOME' ENTERED AT 09:23:35 ON 27 JUL 1999)

FILE 'MEDLINE, EMBASE, CAPLUS, BIOSIS' ENTERED AT 09:36:08 ON 27 JUL 1999

| | | | |
|---|---|---|---|
| L1 | 88877 | S | TRANSGENIC# |
| L2 | 527589 | S | URINE |
| L3 | 1038181 | S | KIDNEY# |
| L4 | 298042 | S | PROMOTER# |
| L5 | 61 | S | L1 AND L2 AND L4 |
| L6 | 26 | DUP REM | L5 (35 DUPLICATES REMOVED) |
| L7 | 41018 | S | DETOXIF? |
| L8 | 1 | S | L1 AND L2 AND L7 |
| L9 | 205003 | S | BLADDER# |
| L10 | 0 | S | L1 AND L7 AND L9 |
| L11 | 198 | S | L9 AND L1 |
| L12 | 56 | S | L4 AND L11 |
| L13 | 24 | DUP REM | L12 (32 DUPLICATES REMOVED) |

L6 ANSWER 10 OF 26 MEDLINE DUPLICATE 5
AN 1998108859 MEDLINE
DN 98108859
TI The bladder as a bioreactor: urothelium production and secretion of growth
hormone into **urine** [see comments].
CM Comment in: Nat Biotechnol 1998 Jan;16(1):21-2
AU Kerr D E; Liang F; Bondioli K R; Zhao H; Kreibich G; Wall R J; Sun T T
CS Gene Evaluation and Mapping Laboratory, Agricultural Research Service, United States Department of Agriculture, Beltsville, MD 20705, USA.
NC DK49469 (NIDDK)
DK39753 (NIDDK)
SO NATURE BIOTECHNOLOGY, (1998 Jan) 16 (1) 75-9.
Journal code: CQ3. ISSN: 1087-0156.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199805
EW 19980503
AB Uroplakin genes are expressed in a bladder-specific and differentiation-dependent fashion. Using a 3.6-kb **promoter** of mouse uroplakin II gene, we have generated **transgenic** mice that express human growth hormone (hGH) in their bladder epithelium, resulting in its secretion into the **urine** at 100-500 ng/ml. The levels of **urine** hGH concentration remain constant for longer than 8 months. hGH is present as aggregates mostly in the uroplakin-delivering cytoplasmic vesicles that are targeted to fuse with the apical surface. Using the bladder as a bioreactor offers unique advantages, including the utility of all animals throughout their lives. Using **urine**, which contains little protein and lipid, as a starting material facilitates recombinant protein purification.

L6 ANSWER 11 OF 26 MEDLINE DUPLICATE 6
AN 1998010664 MEDLINE
DN 98010664
TI The kidney androgen-regulated protein **promoter** confers renal proximal tubule cell-specific and highly androgen-responsive expression on
the human angiotensinogen gene in **transgenic** mice.
AU Ding Y; Davisson R L; Hardy D O; Zhu L J; Merrill D C; Catterall J F; Sigmund C D
CS Genetics Program, University of Iowa College of Medicine, Iowa City, Iowa 52242, USA.
NC HL48058 (NHLBI)
HL55006 (NHLBI)
HD13541 (NICHD)
+
SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1997 Oct 31) 272 (44) 28142-8.
Journal code: HIV. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199802
EW 19980204
AB **Transgenic** mice were generated containing a 1542-base pair fragment of the kidney androgen-regulated protein (KAP) **promoter** fused to the human angiotensinogen (HAGT) gene with the goal of

specifically targeting inducible expression of renin-angiotensin system components to the kidney. High level expression of both KAP-HAGT and endogenous KAP mRNA was evident in the kidney of male mice from two independent **transgenic** lines. Renal expression of the transgene in female mice was undetectable under basal conditions but could be strongly induced by administration of testosterone. Testosterone treatment did not cause a transcriptional induction in any other tissues examined. However, an analysis of six androgen target tissues in males revealed that the transgene was expressed in epididymis. No other extra-renal expression of the transgene was detected. In situ hybridization demonstrated that expression of HAGT (and KAP) mRNA in males and testosterone-treated females was restricted to proximal tubule epithelial cells in the renal cortex. Although there was no detectable human angiotensinogen protein in plasma, it was evident in the **urine**, consistent with a pathway of synthesis in proximal tubule cells and release into the tubular lumen. These results demonstrate that 1542 base pairs of the KAP **promoter** is sufficient to drive expression of a heterologous reporter gene in a tissue-specific, cell-specific, and androgen-regulated fashion in **transgenic** mice.

L6 ANSWER 13 OF 26 CAPLUS COPYRIGHT 1999 ACS
AN 1997:105228 CAPLUS
DN 126:114187
TI Expression of foreign genes in the bladder epithelium and recovery of the gene product in the **urine**
IN Sun, Tung-Tien
PA New York University, USA; Sun, Tung-Tien
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9639494 | A1 | 19961212 | WO 96-US8233 | 19960531 |
| | W: AU, CA, JP, US | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| | US 5824543 | A | 19981020 | US 95-464961 | 19950605 |
| | CA 2221453 | AA | 19961212 | CA 96-2221453 | 19960531 |
| | AU 9659615 | A1 | 19961224 | AU 96-59615 | 19960531 |
| | EP 837931 | A1 | 19980429 | EP 96-916890 | 19960531 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| PRAI | US 95-464961 | 19950605 | | | |
| | WO 96-US8233 | 19960531 | | | |

AB A method for the directing expression of biol. active mols. in the urothelium via use of urothelial-specific **promoters** and a method for producing **transgenic** animals resulting in the synthesis of biol. active mols. that are secreted into their **urine** for subsequent recovery are provided. Specifically, the **promoter** region of the mouse uroplakin II gene is characterized for this use. The **promoter** drives suprabasal cell-specific expression of a reporter gene in **transgenic** mice. The development of mice secreting human growth hormone into the **urine** at concns. of 400-500 ng/mL is reported. The blood concn. of the hormone was <5 ng/mL.

L6 ANSWER 14 OF 26 CAPLUS COPYRIGHT 1999 ACS
AN 1997:6067 CAPLUS
DN 126:27673
TI **Transgenic** multicellular eukaryotes expressing genes for enzymes of post-translational modification of proteins

IN Lubon, Henryk; Morohan, William N.; Paleyanda, [redacted]ha K.
PA American Red [redacted]ss, USA
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 9634966 | A2 | 19961107 | WO 96-US6121 | 19960506 |
| W: AU, CA, JP, MX | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| CA 2220109 | AA | 19961107 | CA 96-2220109 | 19960506 |
| AU 9663474 | A1 | 19961121 | AU 96-63474 | 19960506 |
| PRAI US 95-434834 | | 19950504 | | |
| WO 96-US6121 | | 19960506 | | |

AB **Transgenic** non-human multicellular organisms contg. expression cassettes for enzyme involved in post-translational modification of proteins are described for use in the manuf. of proteins. The **transgenic** organism most often carries genes for enzymes of post-translational modification and the gene for a protein of interest that is a substrate for the modification enzyme. Preferably, the genes are regulated, e.g. by development, tissue-type, or by a chem. inducer and the modified protein is secreted into a bodily fluid. An example provides **transgenic** mice that synthesize human protein C and the processing protease PACE/furin in mammary glands and secrete both proteins into milk. The genes are placed under control of the mammary gland-specific **promoter** of the whey acidic protein gene.

L6 ANSWER 19 OF 26 CAPLUS COPYRIGHT 1999 ACS
AN 1995:229014 CAPLUS
DN 122:1430
TI Metabolism in **transgenic** mice expressing human growth hormone fusion gene driven by **promoter** of mouse whey acidic protein (mWAP/hGH)
AU Nagasawa, Hiroshi; Nagumo, Akiko; Hasegawa, Michiko
CS Fac. Agric., Meiji Univ., Kawasaki, 214, Japan
SO Meiji Daigaku Nogakubu Kenkyu Hokoku (1994), 100, 13-21
CODEN: MDNHA3; ISSN: 0465-6083
DT Journal
LA English
AB Chronic excess secretion of human growth hormone was suggested to induce breast cancer, obesity, and disability in pregnancy in **transgenic** mice of human growth hormone driven by the **promoter** of mouse whey acidic protein (mWAP/hGH Tg mice). The increased rate of body wt. was more in mWAP/hGH Tg mice after 100 days of age than in control mice. Urinary secretion of urea, taurine, and a substance with a 2.88 ppm signal in NMR was significantly less in the male **transgenic** mice than control male mice. The female **transgenic** mice differentiated normally, and induced disability in pregnancy, gestation, and suckling.

L6 ANSWER 20 OF 26 MEDLINE DUPLICATE 10
AN 94176725 MEDLINE
DN 94176725
TI **Transgenic** mouse lines with ectopic expression of alpha-1,3-galactosyltransferase: production and characteristics.
AU Ikematsu S; Kaname T; Ozawa M; Yonezawa S; Sato E; Uehara F; Obama H; Yamamura K; Muramatsu T
CS Department of Biochemistry, Faculty of Medicine, Kagoshima University, Japan..

SO GLYCOBIOLOGY, (1993 Dec) 3 (6) 575-80.
Journal code: [redacted]L. ISSN: 0959-6658.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199406
AB The cDNA of murine alpha-1,3-galactosyltransferase was placed under the control of the beta-actin **promoter** and cytomegalovirus enhancer, then introduced into male pronuclei of fertilized mouse eggs. The three **transgenic** mouse lines obtained were analysed for the expression of the transferase by staining with Griffonia simplicifolia agglutinin I-B4 (GSI-B4), which is alpha-galactosyl specific. Compared with wild-type mice, all lines of **transgenic** mice expressed GSI-B4 binding sites more intensely in the renal tubular brush border and lung alveolar epithelium, and newly expressed them in the photoreceptor outer segments, goblet cells of the small intestine and around spermatogonia. GSI-B4 binding sites were also detected in the liver of some **transgenic** mice. Even though the introduced enzyme gene was expressed in embryos, it did not severely hinder embryogenesis. The **transgenic** mice tended to secrete more proteins in the **urine** than the wild type. Furthermore, low body weights, partial damage to hair growth and early death occurred more frequently in the **transgenic** mice.

L6 ANSWER 24 OF 26 MEDLINE DUPLICATE 12
AN 90368165 MEDLINE
DN 90368165
TI Hypotension in **transgenic** mice expressing atrial natriuretic factor fusion genes [see comments].
CM Comment in: Hypertension 1990 Sep;16(3):308-10
AU Steinhelper M E; Cochrane K L; Field L J
CS Cold Spring Harbor Laboratory, NY 11724..
NC HL-38605 (NHLBI)
CA-46370 (NCI)
HL-07992 (NHLBI)
+
SO HYPERTENSION, (1990 Sep) 16 (3) 301-7.
Journal code: GK7. ISSN: 0194-911X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199012
AB Chronic regulation of the cardiovascular system by atrial natriuretic factor was investigated by generating **transgenic** mice with elevated hormone levels in the systemic circulation. A fusion gene comprising the mouse transthyretin **promoter** and mouse atrial natriuretic factor structural sequences was designed so as to target hormone expression to the liver. Hepatic expression of atrial natriuretic factor was detectable as early as embryonic day 15 in **transgenic** animals. In adult **transgenic** mice, plasma immunoreactive atrial natriuretic factor concentration was elevated at least eightfold as compared with nontransgenic littermates. The mean arterial pressure of conscious **transgenic** mice was 75.5 +/- 0.9 mm Hg, significantly less than that of nontransgenic siblings (103.9 +/- 2.0 mm Hg). This difference in mean arterial pressure was not accompanied by significant changes in several other physiological parameters, including heart rate, plasma and urinary electrolytes, water intake, and **urine** volume. This study demonstrates that a chronic elevation of plasma atrial natriuretic factor decreases arterial blood pressure without inducing diuresis and natriuresis in **transgenic** mice and also illustrates the value of the **transgenic** approach for the study of the cardiovascular system.

L13 ANSWER 20 OF 24 MEDLINE DUPLICATE 11
AN 95148601 MEDLINE
DN 95148601
TI A tissue-specific **promoter** that can drive a foreign gene to express in the suprabasal urothelial cells of **transgenic** mice.
AU Lin J H; Zhao H; Sun T T
CS Ronald O. Perelman Department of Dermatology, Kaplan Comprehensive Cancer Center, New York University School of Medicine, NY 10016..
NC DK39753 (NIDDK)
DK47529 (NIDDK)
AR7190-20 (NIAMS)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1995 Jan 31) 92 (3) 679-83.
Journal code: PV3. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
OS GENBANK-U14421
EM 199505
AB Uroplakins are a group of integral membrane proteins that are synthesized as the major differentiation products of urothelium. The luminal portions of these proteins form 12-nm protein particles arranged in a two-dimensional crystalline array. The expression of uroplakin genes is **bladder** specific and differentiation dependent; little is known, however, about their molecular regulation. Here we describe the cloning of mouse uroplakin II gene and demonstrate, in **transgenic** mouse experiments, that a 3.6-kb 5'-flanking sequence of this gene can drive a bacterial lacZ (reporter) gene to express in the suprabasal cell layers of the urothelium. The transgene was not expressed in any tested (nonurothelial) epithelial and other tissues (except hypothalamus). These results suggest that most of the cis elements that confer the **bladder**-specific and differentiation-dependent expression of mouse uroplakin II gene must reside in the 3.6-kb sequence. The availability of a **promoter** capable of delivering a foreign molecule to the differentiated cell layers of **bladder** epithelium opens avenues for studying normal and pathological urothelial differentiation in **transgenic** mice.